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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/443,863	11/19/1999	INDU PARIKH	401930/SKYE PHARMA	7862
21874	7590	06/23/2004	EXAMINER	
EDWARDS & ANGELL, LLP P.O. BOX 55874 BOSTON, MA 02205			KISHORE, GOLLAMUDI S	
			ART UNIT	PAPER NUMBER
			1615	

DATE MAILED: 06/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/443,863	PARIKH ET AL.	
	Examiner	Art Unit	
	Gollamudi S Kishore, PhD	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 April 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 50-95 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 50-95 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The amendment dated 4-12-04 is acknowledged.

Claims included in the prosecution are 50-95.

Claim Rejections - 35 USC § 103

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
2. Claims 50-95 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 98/07414 cited in the previous action. WO discloses the same process of preparation for the rapidly dispersing oral dosage forms of hydrophobic compounds wherein the particles are coated with at least two surfactants; one of the surfactants is a phospholipid (surface modifying agent). The average particle sizes of the hydrophobic compound are less than 10 microns. The composition contains other claimed materials such as celluloses and mannitol. The process of preparation involves the mixing of the components (water insoluble active agent and the surface modifying agents) in an aqueous medium, sonicating it and lyophilizing the composition to form particles (note the abstract, page 2, line 25 through page 8, line 19, Examples and claims). The process by WO differs from the claimed process in the amended claims in that, the bulking agent is added along with the active agent and the surface modifiers. However, in the paragraph bridging pages 7 and 8, WO teaches subjecting the mixture of the phospholipid and the active agent to procedures such as sonication and homogenization and the goes on to teach that mannitol and other agents may be added to adjust the final formulation to isotonicity as well as a stabilizing agent during drying. It would have been obvious to one of ordinary skill in the

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art from these teachings that the addition of mannitol is a manipulatable parameter, that is, it can be added either before or after the homogenization step with the expectation of obtaining the best possible stabilized product. Instant invention therefore, is an obvious extension of the prior art's teachings. A careful review of instant specification on page 6 indicates that mannitol can be added prior to producing the micronized particles of the therapeutic agent (formulation) or to the homogeneous suspension of micro particles prior to freeze-drying and thus, this step does not appear to be critical.

3. Claims 50-95 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yarwood (5,827,541) by itself or in further combination with Green (5,976,577) of record or Na (5,326,552) or WO 98/07414 cited above by themselves or in combination.

Yarwood discloses a process for the rapidly dispersing oral dosage forms of hydrophobic compounds wherein the particles are coated with a surfactant (surface modifying agent).

The surfactant taught is claimed poloxamer. The average particle sizes of the hydrophobic compound are less than 10 microns. The composition contains other materials such as celluloses and mannitol. The process of preparation involves the mixing of the components and lyophilizing the composition to form particles. (note the abstract, column 1, line 54 through col. 4, line 14, Examples and claims). Yarwood does not disclose phospholipids as the surfactant; Yarwood also does not teach a combination of surfactants. However, it should be pointed out that according to Yarwood on col. 2, line 51 et seq., any surfactant, which fulfills the requirement of pharmaceutical acceptability, may be used. Therefore, it would have been obvious to one of ordinary skill in the art to use phospholipids which are well know surfactants in the process of Yarwood based on this suggestion and from the guidance provided with a reasonable expectation of success.

One of ordinary skill in the art would be further motivated to use phospholipids with the expectation of obtaining at least similar results, in view of the references of Green, and Na and WO all of which teach the use of phospholipids to coat sub-micron size particles just as in instant method (see abstract and col. 5, lines 30-48 of Green; abstract, col. 2, lines 49-53; col. 3, line 65 through col. 4, line 38 of Na). What is also lacking in Yarwood, is the teaching of the addition of mannitol as a separate step. However, since Yarwood is directed to rapidly dispersing oral dosage form same as in instant method, it is deemed obvious to one of ordinary skill in the art to manipulate the basic method of Yarwood with the expectation of obtaining the best possible results. Furthermore, as pointed out above, in the paragraph bridging pages 7 and 8, WO teaches subjecting the mixture of the phospholipid and the active agent to procedures such as sonication and homogenization and the goes on to teach that mannitol and other agents may be added to adjust the final formulation to isotonicity as well as a stabilizing agent during drying. It would have been obvious to one of ordinary skill in the art from these teachings that the addition of mannitol is a manipulatable parameter, that is, it can be added either before or after the homogenization step with the expectation of obtaining the best possible stabilized product. Instant invention therefore, is an obvious extension of the prior art's teachings. A careful review of instant specification on page 6 indicates that mannitol can be added prior to producing the micronized particles of the therapeutic agent (formulation) or to the homogeneous suspension of micro particles prior to freeze-drying and thus, this step does not appear to be critical.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant argues that Yarwood provides no guidance for selecting any other

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surfactant, other than it should be pharmaceutically acceptable. According to applicant therefore, one skilled in the art would be force to conduct an expensive and time-consuming iterative process. This argument is not found to be persuasive since phospholipids are known pharmaceutically acceptable surfactants and therefore, one would select this surfactant with a reasonable expectation of success.

Applicant argues that Na is not in the same field of Yarwood and it is non-analogous art. The examiner disagrees since Na is directed to therapeutic compositions of nanoparticles (see col. 3, lines 25-27) same as Yarwood and in instant invention and therefore, relevant art. Applicant's arguments with regard to particle sizes of less than 400 nm in Na are not found to be persuasive since Na is combined to show that phospholipids are commonly used surfactants to coat nanoparticles. Furthermore, on col. 3, lines 33-45 Na teaches that coarse particles can be reduced in size using conventional milling method and therefore, one of ordinary skill in the art would be motivated to prepare particles of desired sizes.

Applicant's arguments with regard to Green are not found to be persuasive. Applicant once again argues that Green is not in the same field. According to applicant that Green is concerned with delaying the release of drug. The examiner disagrees and points out Green is directed to rapidly disintegrating oral dosage forms (see the title and abstract) and therefore in the same field. Applicant's arguments with regard to the teachings of coated and uncoated particles and the sizes are not persuasive since as pointed above with regard to Na, Green is combined to show that phospholipids are known surfactants. The primary reference teaches the claimed particle sizes and they are coated.

1. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

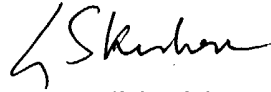
A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S Kishore, PhD whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For

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more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Gollamudi S Kishore, PhD
Primary Examiner
Art Unit 1615

GSK